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| 10/590,211 | 08/22/2006 | Jean-Marie Buerstedde | P30753US00 | 5528 |

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ARNOLD & PORTER LLP
ATTN: IP DOCKETING DEPT.
555 TWELFTH STREET, N.W.
WASHINGTON, DC 20004-1206

| EXAMINER | |
|---|---|
| SAJJADI, FEREYDOUN GHOTB | |
| ART UNIT | PAPER NUMBER |
| 1633 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/590,211 | BUERSTEDDE ET AL. | |
| | Examiner | Art Unit | |
| | Fereydoun G. Sajjadi | 1633 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *22 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-43* are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

Claims 1-43 introduced by the amendment dated August 22, 2006 are pending in the application.

### *Election/Restrictions*

Restriction is required under 35 U.S.C. 121 and 372.

1. This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1-27, drawn to a genetically modified lymphoid cell having gene conversion fully or partially replaced by hypermutation, wherein said cell has no deleterious mutations in genes encoding paralogues and analogues of RAD51.

Group II, claim(s) 28, drawn to a non-human transgenic animal containing a lymphoid cell having gene conversion fully or partially replaced by hypermutation, wherein said cell has no deleterious mutations in genes encoding paralogues and analogues of RAD51

Group III, claim(s) 29-31 and 35, drawn to a method for preparing a cell capable of directed and selective genetic diversification of a target nucleic acid by hypermutation, comprising transfecting a lymphoid cell capable of gene conversion with a target nucleic acid and identifying a cell having the endogenous V-gene replaced with the target nucleic acid.

Group IV, claim(s) 29 and 32, drawn to a method for preparing a cell capable of directed and selective genetic diversification of a target nucleic acid by hypermutation, comprising transfecting a lymphoid cell capable of gene conversion with a target nucleic acid and identifying a cell having the endogenous V-gene replaced with the target nucleic acid, and transfecting the identified cell with a further genetic construct comprising a reporter gene.

Group V, claim(s) 29, and 33-34, drawn to drawn to a method for preparing a cell capable of directed and selective genetic diversification of a target nucleic acid by hypermutation, comprising transfecting a lymphoid cell capable of gene conversion with a target nucleic acid and identifying a cell having the endogenous V-gene replaced with the target nucleic acid, and transfecting the identified cell with a further genetic construct comprising a reporter gene, further comprising the conditional expression of a trans-acting regulatory factor.

Group VI, claim(s) 36-37, 39 and 42-43, drawn to a method for preparing a gene product having a desired activity, comprising the steps of culturing genetically modified lymphoid cells having gene conversion fully or partially replaced by hypermutation, comprising an expressed target

nucleic acid, identifying a cell which expresses a mutated gene product having the desired activity, and selecting a cell expressing a gene product having an improved desired activity.

Group VII, claim(s) 36, 38 and 40-41, drawn to a method for preparing a gene product having a desired activity, comprising the steps of culturing genetically modified lymphoid cells having gene conversion fully or partially replaced by hypermutation, comprising an expressed target nucleic acid, identifying a cell which expresses a mutated gene product having the desired activity, and selecting a cell expressing a gene product having an improved desired activity, further comprising the step of switching off genetic diversification.

37 CFR 1.475 (e) states:
"The determination whether a group of inventions is so linked as to form a single general inventive concept shall be made without regard to whether the inventions are claimed in separate claims or as alternatives within a single claim."
In view of 37 CFR 1.475 (e), Groups III-V and VI-VII are considered a plurality of the inventions listed in claims 29 and 36, respectively.

The inventions listed as Groups I-VII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

According to PCT Rule 13.2, unity of invention exists only when a shared same or corresponding special technical feature is a contribution over the prior art. The technical feature, which is shared by Groups I-VII, is a genetically modified lymphoid cell having gene conversion fully or partially replaced by hypermutation. Groups I-VII do not share a special technical feature over the art because the inventions lack an inventive step under PCT Article 33(3) as being obvious over Sale et al. (U.S. Patent Publication No.: 2005/0026246; filed Dec. 11, 2003). Sale et al. teach a cell line capable of directed hypermutation of a specific nucleic acid region (Abstract), wherein the cell is an immunoglobulin-expressing or lymphoid cell (claims 3 and 7), and wherein a nucleic acid encoding a heterologous desired gene activity and is expressed (claim 22). As the cells constitute the Ramos cell line and derivatives thereof, the cells do not have deleterious mutations in the genes encoding paralogues and analogues of the RAD51 protein.

The claims in Groups I-VII are drawn to distinct products and methods that utilize distinct steps, requiring non-coextensive search and examination. Thus, it follows from the preceding analysis that the claimed inventions listed as Groups I-VII do not relate to a single

inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding technical features for the reasons set forth above.

MPEP 1893.03(d) states: If an examiner (1) determines that the claims lack unity of invention and (2) requires election of a single invention, when all of the claims drawn to the elected invention are allowable (i.e., meet the requirements of 35 U.S.C. 101, 102, 103 and 112), the nonelected invention(s) should be considered for rejoinder. Any nonelected product claim that requires all the limitations of an allowable product claim, and any nonelected process claim that requires all the limitations of an allowable process claim, should be rejoined. See MPEP § 821.04 and § 821.04(a). Any nonelected processes of making and/or using an allowable product should be considered for rejoinder following the practice set forth in MPEP § 821.04(b).

2. This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are as follows:

A specifically named single species of animal from which the cells are derived, from the species of chicken, sheep, cow, pig or rabbit, as recited in claim 6.

A specifically named single species of genetic diversification, from the species of hypermutation or a combination of hypermutation and gene conversion, as recited in the specification and claims 10 and 28.

A specifically named single species of target nucleic acid, from the species of an immunoglobulin chain, V-gene, a selection marker, a DNA-binding protein, an enzyme, or a receptor protein, as recited in claims 12 and 13.

A specifically named single species of transcription regulatory element or RNAi sequence, as recited in the claim 14.

A specifically named single species of selection, from the species of activity of the target nucleic acid within the cell, on the cell surface, or outside the cell, as recited in the claim 19.

A specifically named single species for modulation, from the species of varying the number, the orientation, the length or degree of homology of the gene conversion donors or by a trans-acting regulatory factor, as recited in claims 23 and 24.

A specifically named single species of transacting regulatory factor, such as the species of AID, or a specific DNA repair or recombination factor, as recited in the claims 24-26, 33, 34 and 40-41.

Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

The claims are deemed to correspond to the species listed above in the following manner:

Claims 1, 27, 28, 29 and 36, and claims dependent therefrom correspond to all the species listed above.

The following claim(s) are generic: 1-43.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: As the technical features (hypermutation, immunoglobulin chain, V-gene, a selection marker, a DNA-binding protein, an enzyme, transcription regulatory element or RNAi, activity of the target nucleic acid within the cell, on the cell surface, or outside the cell, varying the number the orientation, the length or degree of homology of the gene conversion donors or by a trans-acting regulatory factor, AID, or a specific DNA repair or recombination factor) linking the members do not constitute a special technical feature as defined by PCT Rule 13.2, particularly since each of the species does not share a substantially common structural feature, the requirement for unity of invention is not fulfilled.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fereydoun G. Sajjadi whose telephone number is (571) 272-3311. The examiner can normally be reached on 7:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Fereydoun G. Sajjadi, Ph.D.
Examiner, A.U. 1633

*/Anne Marie S. Wehbé/*
Primary Examiner, A.U. 1633